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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,713	08/05/2003	Joseph Armand Picard	PC25298A	8942
28880	7590	01/03/2006	EXAMINER	
WARNER-LAMBERT COMPANY 2800 PLYMOUTH RD ANN ARBOR, MI 48105			BALASUBRAMANIAN, VENKATARAMAN	
			ART UNIT	PAPER NUMBER

1624

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/634,713		PICARD, JOSEPH ARMAND	
	Examiner		Art Unit	
	Venkataraman Balasubramanian		1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/8/04, 7/5/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-9 and 11-14 drawn to a compound of formula I wherein D is pyrazinone or formula II or IV, composition and method of use in the reply filed on 10/7/2005 is acknowledged. Cancellation of non-elected subject matter and election of first species of claim 9 is also acknowledged. Claims 1-9, 11 and 13 are now pending.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i). The traversal is on the ground(s) that it is not a serious burden search and the instant invention has common structural element.

Information Disclosure Statement

References cited in the Information Disclosure Statements, filed on 3/8/2004 & 7/5/2005, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

Art Unit: 1624

which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and shares the same indefiniteness.

1. In claim 1, the definition of D renders claim 1 and its dependent claims 2-9, 11 and 13 indefinite as the definition of D is vague and unclear. Note the second choice of D definition includes what is already recited in the first choice. See for example $C=C-CH_2$ which is also included in the first choice. In addition, it is not clear what is the point of attachment of the D choices.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 11 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for $Q = CH(R^6)CO$ or $CH(R^6)CS$, as substituents on nitrogen of pyrazinone, does not reasonably provide enablement for S-radical linked, N-radical linked and C+C radical linked substituents on the said nitrogen as recited for compound of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Note dependent claims 2-8, 11 and 13 are also rejected herein as they depend on the rejected claim 1 and shares the same lack of scope of enablement.

In evaluating the enablement question, following factors are considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include:

Art Unit: 1624

1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to compound of formula shown in claim 1, formula II and IV wherein the D is a pyrazinone. Claim 1 permits various Q choices which can be CH linked to the nitrogen of pyrazinone as well heteroatoms linked to the nitrogen and a alkynyl linked to the nitrogen. Specification is not adequately enabled as to how to make compounds of formula shown in claim 1, formula II or formula IV wherein the above said groups are variously substituted heteroatoms linked to the nitrogen and a alkynyl linked to the nitrogen. The Scheme 3 of page 11 is pertinent to making compound wherein CH linked to the nitrogen of pyrazinone compounds and not for the above said groups.

Specification offers no teachings or suggestion as to how to make the make such compounds.

2. The predictability or lack thereof in the art:

The process of the Scheme 3 as applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s) to make these claimed compounds.

4. The amount of direction or guidance present:

Examples illustrated in the experimental section or written description offer no guidance or teachings as to how make these compounds when the Q is through a CH linkage to the nitrogen, and there are working examples for other choices stated above.

5. The presence or absence of working examples:

Although examples on pages 119-125 show enablement for sixty compounds, they are limited to compounds with CH linkage. There are no representative examples showing the viability of the process for the reactive choices stated above embraced in the instant claims.

6. The breadth of the claims:

Specification has no support, as noted above, for all compounds generically embraced in the claim language would lead to desired compound of formula I with said reactive linkage groups and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward the reaction to make such compounds.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula shown in claim 1 in view of the general reactivity of these groups.

Art Unit: 1624

Thus, factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. have been demonstrated to be sufficiently lacking in the case for the instant claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for treating osteoarthritis or rheumatoid arthritis with compounds of claim 9, does not reasonably provide enablement for any or all Q choices and other variables generically embraced in the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and shares the same limitation.

Representative examples of structurally diverse compounds generically embraced in the invention are not shown to possess in vitro activity much less in vivo uses claimed herein. Instant genus of triazine compound embrace compounds with substituents bearing plethora of structural cores and functional groups and other groups permitted at instant variables which include various choices of Q for both ends, variously substituted monocyclic rings, bicyclic rings, rings with variable ring sizes and variable heteroatoms variety of reactive functional groups such COOH, OH, SH, amido, sulfoxides, sulfones nitrile, carbamates etc. There is no reasonable basis for assuming

Art Unit: 1624

that the myriad of compounds embraced by the claims will all share the same bioactivity profile since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive art such as the pharmaceuticals.

Note *Ex parte Gelles* 22 USPQ 2nd 1318, especially the following quote: "The evidence relied upon also should be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to prior art subject matter."

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method of use. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Prophylactics

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from

Art Unit: 1624

8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian
Venkataraman Balasubramanian

12/26/2005